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The Association Between Obstructive Sleep Apnea and Arrhythmias

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Abstract

Obstructive sleep apnea (OSA) is caused by intermittent episodes of partial or complete closure of the upper airway, leading to apneic episodes while the patient is asleep. Atrial fibrillation (AF) has more than 750,000 hospitalizations per year and accounts for an estimated 130,000 deaths each year. The death rate from AF as the primary or a contributing cause of death has been rising for more than two decades. The material reviewed in this paper focuses on the association between OSA and arrhythmias. It goes into detail regarding epidemiology, pathophysiology, types of arrhythmias, and therapies seen in association with OSA.

Categories: Pulmonology
Keywords: obstructive sleep apnea, arrhythmias, atrial fibrillation, continuous positive airway pressure therapy

Introduction And Background

Sleep-disordered breathing (SDB) is a cumulative term for sleep-related breathing disorders and abnormalities of respiration during sleep. SDB consists of obstructive sleep apnea (OSA), central sleep apnea syndrome, sleep-related hypoventilation disorder, sleep-related hypoxemia, primary snoring, and catathrenia. OSA is caused by intermittent episodes of partial or complete closure of the upper airway, leading to apneic episodes while the patient is asleep [1]. OSA is diagnosed by a combination of positive patient history and positive findings on polysomnography. An apnea-hypopnea index (AHI) of greater than five is diagnostic of OSA.

Review

Epidemiology

The incidence and prevalence of OSA vary based on age in the general population. The prevalence is higher in the middle-aged and advanced age populations [2]. Based on an AHI of more than five, the prevalence ranges from 9%-38% and is higher in men than in women [2]. At an AHI of more than 15, the prevalence in the general adult population ranged from 6%-17% and was 49% in the advanced age group [2].

Atrial fibrillation (AF) has a prevalence of 9% in the 65 years and above population as compared to the 2% prevalence in the younger than 65 years population [3]. An estimated 2.7-6.1 million people in the United States have AF [3]. AF has more than 750,000 hospitalizations per year and accounts for an estimated 130,000 deaths each year [4-5]. Medical costs for AF patients are

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about $8,705 higher than for people without AF [3,6]. The death rate from AF as the primary or a contributing cause of death has been rising for more than two decades [4-5].

Pathophysiology

Over the years, attempts have been made to determine how arrhythmias develop in OSA patients. In OSA, the frequent collapse of the airway causes oxyhemoglobin desaturation, which leads to persistent inspiratory efforts made against a collapsed airway, often resulting in the patient's arousal from sleep [1].

One hypothesis is that OSA has reduced blood oxygen and increased carbon dioxide levels due to problems with the baroreflex and chemoreflex activity, leading to the activation of the sympathetic nervous system, causing electrical remodeling of the heart [7-10]. This remodeling can lead to arrhythmia development [1,7-10].

Another hypothesis is that co-existing hypertension in OSA patients may be responsible for the development of AF. Past studies have shown a strong association between OSA and hypertension, as well as hypertension and AF. Hypertension has been shown to cause atrial remodeling. Similarly, in OSA patients with hypertension, it is hypothesized that persistent inspiratory efforts made against a collapsed airway cause dramatic shifts in intracardiac pressures, leading to the activation of atrial ion channels, thus creating an acute change in cardiac chamber dimensions [11-12]. This change in size can lead to AF development [11-12].

The third hypothesis is the OSA effect of applying negative intrathoracic pressure on both atrial and ventricular free walls, which will lead to cardiac stretching thus activating cardiac ion channels, causing a change in cardiac chamber size, which can lead to arrhythmias [13].

The fourth hypothesis is related to OSA causing hypoxemia that stimulates the vagal nerve, leading to cardiac vagal reflex activation. In approximately 10% of OSA patients, the resulting hypoxemia activates the cardiac vagal reflex, leading to the development of bradyarrhythmias even in the absence of cardiac conduction disease [14].

Types of arrhythmias

Different types of arrhythmias may be found in patients of OSA. Based on past research studies (see Table *1*), there are several observed associations between OSA and arrhythmias.

Author Name of Research Study	Study Population	Relationship Between Sleep-Disordered Breathing and Arrhythmias
Atrial fibrillation		
Mehra et al. [15]	566 patients	Study contained 228 patients with OSA and 338 patients without OSA. AF seen in 4.8% of patients. It was determined that severe OSA will have two to four higher chances of developing complex arrhythmias.
Gami et al. [16]	524 patients	Study contained 151 patients with AF and 312 patients with other Cardiovascular Disease (CVD). The prevalence of OSA was higher in patients with AF than in the opposing group.
Porthan et al. [17]	115 patients	OSA was common in lone AF patients. The study could not demonstrate that OSA was more common in AF patients than in corresponding controls.

Javaheri et al. [18]	81 patients	AF was seen in 32% of patients. All patients were male, ambulatory, with stable HF, and had LVEF below 45%.
Flemos et al. [19]	263 patients	Patients having sleep apneas were found to have a low prevalence.
Mooe et al. [20]	121 patients	AF in 32% of patients with AHI more than five. Furthermore, AF was found in 18% patients with AHI less than five.
Sick sinus syndrome		
Simantirakis et al. [21]	23 patients	Rhythm disturbances were seen in 48% of patients. They consisted of frequent episodes of bradycardia and long pauses, which were observed in patients who had moderate to severe OSA.
Garrigue et al. [22]	98 patients	There was a high prevalence of undiagnosed OSA in the patients. It was 59% and all patients had pacemakers.
Grimm et al. [23]	12 patients	The study was conducted with patients who had ventricular asystole and OSA. It was concluded that there was no significant association of sinus node and AV node abnormalities with OSA.
Steiner et al. [24]	12 patients	All patients had Heart Failure. There was no correlation observed between patients having mild sleep apnea and sinus abnormalities.
Velasco et al. [25]	190 patients	The Berlin questionnaire was used during the study. It was concluded that patients at high risk for OSA did not have an increased prevalence of bradyarrhythmias.
Atrioventricular Block		
Becker et al. [26]	239 patients	In about 30% of patients with sleep apnea, there is sinus arrest and AV block.
Sudden cardiac death		
Gami et al. [27]	10,701 patients	All patients had OSA. Compared to the general population SCD is prevalent in OSA patients.
Gami et al. [28]	112 patients	All patients included suffered from SCD. There is a strong association between SCD and OSA.

TABLE 1: Summary of Incidence and Prevalence of OSA and Arrhythmias

OSA: obstructive sleep apnea; AF: atrial fibrillation, HF: heart failure; SAS: sleep apnea syndrome; SCD: sudden cardiac death; LVEF: left ventricular ejection fraction; AHI: apnea-hypopnea index

Atrial fibrillation is a commonly seen arrhythmia in OSA patients [1]. AF occurs when disordered atrial electric activity causes an abnormal electrical rhythm that replaces the normal sinus mechanism [29]. It can be caused by hypertension, myocardial infarction, hyperthyroidism, caffeine use, abnormal heart valves and is seen in sleep apnea patients. AF often goes undiagnosed for a long time because 10%-40% of AF patients are asymptomatic [30]. Symptomatic patients will present with palpitations, shortness of breath, exercise intolerance, chest pain, or malaise [29]. AF is responsible for an estimated 130,000 deaths per year and for the worsening morbidity in other diseases like stroke and heart failure [4-5,30]. AF is found in

two percent of the general population, with an increasing prevalence to 9% in the above 65 years population [3,30].

Sick sinus syndrome (SSS) refers to a collection of disorders marked by the heart's inability to perform its pacemaking function [31]. SSS mostly affects older adults and consists of bradyarrhythmias with or without accompanying tachyarrhythmias [31]. At least 50% of SSS patients develop alternating bradycardia and tachycardia, also known as Tachy-Brady syndrome [31]. SSS results from degenerative fibrosis, ion channel dysfunction, and the remodeling of the sinoatrial node [31]. Signs and symptoms are often subtle early on and become more obvious as the disease progresses [31]. They are commonly related to end-organ hypoperfusion, like syncope secondary to cerebral hypoperfusion [31].

Atrioventricular block (AV block) is an arrhythmia that is caused by a delay or disturbance in the transmission of an electrical impulse from the atria to the ventricles [32]. This can be due to an anatomical or functional impairment in the heart’s conduction system [32]. In general, there are three degrees of AV nodal blocks: first-degree, second-degree (Mobitz type 1 or 2), and third-degree [32]. The causes of AV blocks are myocardial infarction, post-cardiac surgery, electrolyte imbalances, idiopathic fibrosis, and medications that slow atrioventricular conduction [32]. Patients may be asymptomatic or they may present with palpitations, syncope, and dizziness.

Sudden cardiac death is defined as natural death due to cardiac causes, which will present as an abrupt loss of consciousness within the first hour of symptoms [33]. The mechanisms can be ventricular fibrillation, ventricular tachycardia, and flutter with subsequent ventricular fibrillation, torsades de pointes, and, lastly, bradyarrhythmias and asystolic arrest [33].

Treatment

There are no conclusive epidemiologic or longitudinal intervention studies that relate specifically to the prevalence, severity, and consequences of cardiac arrhythmias and the effects of OSA treatment [1]. Despite this, there have been many observations made from previous studies regarding the effectiveness of continuous positive airway pressure (CPAP) therapy for OSA patients and their therapeutic effect on arrhythmia incidence in the same patients. Based on the studies (see Table *2*), CPAP therapy had an effect on reducing the incidence and prevalence of cardiac arrhythmias in OSA patients.

Author Name of Past Study	Study Population	Observations Made Based on the CPAP Therapeutic Effect
Kufoy et al. [34]	39 patients	It was reported that mean AHI for all 39 participants within the sample was 48.54, with heart rate variability decreasing after CPAP was employed for only one night. These results allowed the conclusion to be made that after only one night of CPAP treatment, patients with significant cases of OSA experienced a substantial resolution of cardiac variability.
Becker et al. [26]	239 patients total	It was revealed that seven percent of 239 (17 patients) with OSA had significant bradyarrhythmias and of these 17 patients, only one continued to experience bradyarrhythmias after CPAP therapy.
Simantirakis et al. [21]	23 patients	An observation was made that treating OSA patients with CPAP resulted in a reduction of subsequent cardiac rhythm variations.
Ryan et al. [35]	18 patients	A randomized control trial where 18 OSA patients with heart failure and more than 10 VPB were tested with CPAP therapy. The results showed that the treatment of OSA in those patients reduced the frequency of VPB by 58% during sleep.
Kurlykina et al. [36]	19 patients	Patients were examined and treated with CPAP causing AHI to become decreased from 60.7 episodes per hour to only 5.5 episodes per hour.
Kanagala et al. [37]	43 patients	Observational data put forward by Kanagala et al. showed an increased rate of recurrence (82%) of AF after successful cardioversion in inadequately treated OSA patients as compared with non-OSA and well-treated OSA patients.
Harbison et al. [38]	45 patients	The study investigated the prevalence of significant cardiac rhythm disturbances in 45 patients with established moderate to severe OSA and assessed the impact of nasal CPAP therapy. The treatment results showed a complete resolution of previously observed rhythm disturbances in seven out of eight patients.
Marin et al. [39]	1,651 total patients	Marin et al. was a prospective cohort study that sought to determine the effect of OSA as a cardiovascular risk factor and the potential protective effect of CPAP treatment. At the end of the study, it was determined that in men, severe OSA significantly increases the risk of fatal and non-fatal cardiovascular events. CPAP treatment reduces this risk.

TABLE 2: Observed Therapeutic Effect of CPAP Treatment on Patients with Both Arrhythmias and OSA

AHI: Apnea-hypopnea index; CPAP: continuous positive airway pressure; OSA: obstructive sleep apnea; VPB: ventricular premature beats

Conclusions

The material reviewed in this paper focuses on the association between OSA and arrhythmias. It goes into the details regarding the epidemiology, pathophysiology, and types of arrhythmias seen in association with OSA. It also addresses observations regarding CPAP therapy in reducing arrhythmias. Despite these key points being addressed, larger and more prospective studies are needed to understand the true benefits of CPAP therapy. This is a review article for busy, practicing physicians to have a cumulative view of our current situation regarding the

need for CPAP therapy in patients of both OSA and arrhythmias.

Additional Information

Disclosures

Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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